Behavioural Brain Research: Do people with Parkinson's disease look at task relevant stimuli when walking? An exploration of eye movements

David Hunt (MRes) [1], Samuel Stuart (PhD) [1], Jeremy Nell (MRes) [1], Jeffrey M. Hausdorff (PhD) [2,3,4], Brook Galna[1,5] (PhD), Lynn Rochester (PhD) [1,6], Lisa Alcock (PhD) [1]

[1] Institute of Neuroscience/ Institute for Ageing, Newcastle University, United Kingdom.

[2] Center for the study of Movement, Cognition and Mobility, Neurological Institute, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel.

[3] Rush Alzheimer's Disease Center and Department of Orthopaedic Surgery, Rush University Medical Center, Chicago, Illinois, United States of America

[4] Sagol School of Neuroscience and Department of Physical Therapy, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

[5] School of Biomedical Sciences, Newcastle University, Newcastle upon Tyne, United Kingdom.

[6] The Newcastle upon Tyne NHS Foundation Trust, Newcastle upon Tyne, United Kingdom.

Correspondence:

Dr Lisa Alcock

Brain and Movement Research Group,

Clinical Ageing Research Unit, Campus for Ageing and Vitality,

Institute of Neuroscience/Newcastle University Institute of Ageing

Newcastle University

Newcastle upon Tyne, NE4 5PL

Tel: +44 (0) 191 208 1283 E-mail: lisa.alcock@newcastle.ac.uk

Acknowledgements and Funding

The authors would like to thank Dr. Sue Lord for a critical appraisal of this manuscript prior to submission. This research is supported by the National Institute for Health Research (NIHR) Newcastle Biomedical Research Unit and centre based at Newcastle upon Tyne Hospitals NHS Foundation Trust and Newcastle University. The research was also supported by NIHR Newcastle CRF Infrastructure funding. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health. This work was supported by the VTIME project which is a European Union 7th Framework Programme (FP7) under the Health theme (FP7 - 278169).

David Hunt, Samuel Stuart, Jeremy Nell, Jeffrey M. Hausdorff, Brook Galna, Lynn Rochester and Lisa Alcock have no competing interests.

Behavioural Brain Research: Do people with Parkinson's disease look at task relevant stimuli when walking? An exploration of eye movements

Abstract

Eye movements are impaired by Parkinson's disease (PD) although limited research has explored if PD affects the relevance of visual fixations when walking. Visual fixations may provide crucial contextual information for safe navigation and important insights into fall risk. This study aimed to: investigate visual fixations made while walking under a range of conditions in PD; identify their task relevance; and explore their relationship with clinical features. Thirty-eight people with mild-moderate PD and forty age-matched control participants completed a straight walk with (i) no additional stimuli and (ii) with additional stimuli (visual cues or a high contrast obstacle), whilst wearing a mobile eye-tracker. Fixations were extracted and classified by location and relevance. PD participants made proportionally fewer task-relevant fixations (floor, walls and additional stimuli ahead), caused by significantly more task-irrelevant fixations (floor, walls and ceiling away from waking path) during normal walking (p=0.014). These group differences were not apparent with visual cues (p=0.359). During obstacle crossing trials, PD made significantly more task-relevant fixations than controls (p=0.007). Reduced bilateral visual acuity was associated with fewer fixations in PD. Our findings suggest that people with PD visually explore complex environments less efficiently likely owing to underlying PD pathology. Visual exploration improved with the addition of salient stimuli (for example visual cues or an obstacle) and thus developing and optimising visual interventions could prove critical to improving locomotor safety and reducing falls risk in home environments.

Keywords: Visual Exploration; Eye-Tracking; Gait; Visual cues; Obstacle crossing

1. Introduction

Parkinson's disease (PD) is a movement disorder with increasingly recognised visual impairments [1]. Changes in visual function include: reduced visual acuity and contrast sensitivity due to retinal pathology [2], visuospatial impairments due to changes within the dorsal stream of vision [3], and abnormalities in visual sampling (decreased saccadic frequency) [4]. Impairment in the acquisition, processing and interpretation of incoming visual information has the potential to affect safe locomotion and increase falls risk.

Acquiring information about the visual scene is achieved by a combination of saccades and fixations. Saccades are fast eye movements whereby the fovea shifts between different areas of interest, and these are interspersed with fixations, in which visual information is gathered from the environment [5]. People with PD display abnormalities in saccadic control including deficits in saccade suppression and control of saccade direction [6]. A reduced saccadic frequency has also been noted in people with PD when walking, particularly under dual (cognitive) task conditions and during the early approach phase of straight walking prior to turning compared to age-matched controls [4,7]. People with PD also require more saccades to complete static computer-based trials assessing visuo-cognition [8]. Saccadic deficits in people with PD may influence fixations and as a consequence acquisition of contextual information needed for efficient navigation, however this is currently unclear. While limited evidence suggests that saccades are slower [9] and fixations are longer in people with PD [10], the relevance of the visual information will depend upon fixation location. Moreover, disease severity plays a role with fewer fixations observed in people with more severe PD [11]. Considering the degenerative influence of PD pathology on attentional capacity, the authors concluded that this reduced fixation count was attributed to an attentional overload when navigating complex environments [11].

Visual information is processed and interpreted in pathways radiating from the occipital lobes [12], and these are likely to be affected by PD pathology [3]. Interpreting visual information regarding the surrounding environment is, in part, dependent on the clarity of the visual information acquired (i.e. acuity and contrast sensitivity). In addition, people with PD demonstrate a reduced ability to inhibit irrelevant and prioritise important visual information from reflexive saccades which will influence the acquisition of visual information

[6,13]. Visual interventions for gait impairment in PD, such as visual cues, are prescribed clinically by physiotherapists to overcome gait hypokinesia and restore appropriate spatial scaling during walking [14]. The mechanism underpinning the response to visual cues in PD is not fully understood. Visual cues appear to redirect both vision and attention to relevant environmental stimuli and act as an external visual prompt to regulate and improve gait in PD [10]. Visual cues have been reported to increase the total number of fixations during walking in people with PD [11], however this study did not include a control group so inferences are limited. Interventions to improve locomotor safety are often prescribed to people with PD to overcome pathology-associated gait impairment and reduce trips and falls which are common [15]. Improving the saliency of ground-based obstacles and other trip hazards may work similarly to visual cues by redirecting attention to areas pertinent for safe locomotion. Investigating the contextual relevance of the visual information obtained from fixations exhibited during locomotion (i.e. what participants are looking at and its relevance to the task) could provide insight into one of the mechanisms underlying gait impairment in PD and may contribute to the development of effective interventions to reduce falls risk.

The present study aimed to: 1) identify and classify fixations during walking according to relevance to the task (i.e. Task Relevant or Task Irrelevant), 2) examine the effect of visual cues and obstacles on the task relevance of fixations when walking, and 3) examine whether clinical outcomes (disease specific, visual and cognitive function) are associated with visual exploration in people with PD. We hypothesised that: 1) PD participants would make a lower proportion of task relevant fixations when walking (i.e. due to fewer task relevant fixations and/or more task irrelevant fixations), 2) visual cues and a salient obstacle would increase the proportion of relevant fixations made, and 3) differences in task relevance of fixations would be associated with by visual function, global cognition and PD-specific measures.

2. Materials and methods

2.1 Participants

This study included 41 PD and 41 healthy older adult (control) participants. Data were obtained and collated from two pre-existing data sets: Study 1 (VFDG 'Visual function during gait' [16]) and Study 2 (V-TIME 'Virtual-reality treadmill training to improve mobility and reduce falls in the elderly' [17,18]). The PD cohort were recruited through movement disorder clinics, and controls were identified through local community partnerships. NHS ethical approval was granted for both studies (REC Ref: V-TIME: 12/NE/0249, VFDG: 13/NE/0128), and informed written consent was obtained according to the Declaration of Helsinki [19].

2.2 Inclusion and exclusion criteria

PD participants were recruited providing that they: had a formal diagnosis of PD (UK Brain Bank Criteria)[20], were currently taking antiparkinsonian medication, and were of mild-to-moderate disease severity (Hoehn & Yahr stages I-III) [21]. PD and control participants were included in the study provided they were: >50 years old, able to ambulate unassisted for at least five minutes, and had stable medication for the month prior to assessment. Participants were excluded if they presented with uncorrected visual or auditory deficits and any psychiatric or neurological disorder (other than PD). Severe cognitive impairment (i.e. dementia) was screened for and excluded using the Mini-Mental State Exam (MMSE) [22] (<24/30 for both groups). PD participants were assessed while optimally medicated approximately one hour after taking their antiparkinsonian medication. 68% of the PD cohort had experienced at least one fall within the last 12 months (28 of 41) whereas none of the control group had fallen.

2.3 Outcome measures

Demographic data were collected from participants (age, sex, education) in combination with measures of global cognition (MMSE), visual function (visual acuity and contrast sensitivity) and PD disease severity (disease duration, Hoehn & Yahr stage [21], Unified Parkinson's Disease Rating Scale part III (UPDRS-III) [23]. Monocular and bilateral visual acuity (LogMAR) and contrast sensitivity (Mars CS, Mars Perceptix, NY) were measured following the manufacturers' procedures, using a different chart in each test (three in total) to

avoid learning effects. Differences in left/right visual acuities may interfere with depth perception during navigation [24], so the absolute difference was calculated (left minus right). The modified Falls Efficacy Scale (FES-I) was used to assess fear of falling in the PD group only with higher scores indicating a greater fear of falling [25].

2.4 Protocol

Participants completed two walking conditions at a self-selected pace: (i) walking and (ii) walking with additional stimuli (visual cues or an obstacle) (Figure 1A). Both study cohorts completed the straight walking trials and only data for this walking condition were combined. For the visual cueing trial (Study 1), five parallel lines of black tape were affixed directly onto the light coloured floor surface. The lines were perpendicular to the trial pathway and started from 150-cm into the walk separated by 50-cm. For the obstacle crossing trial (Study 2), a high contrast (yellow) obstacle (HxWxD 15x60x2cm) was placed half way down the walking path. All walking trials were completed over a 10-metre walkway. Trial order was counterbalanced and each trial was completed three times. The laboratory was well lit which remained consistent during all testing sessions.

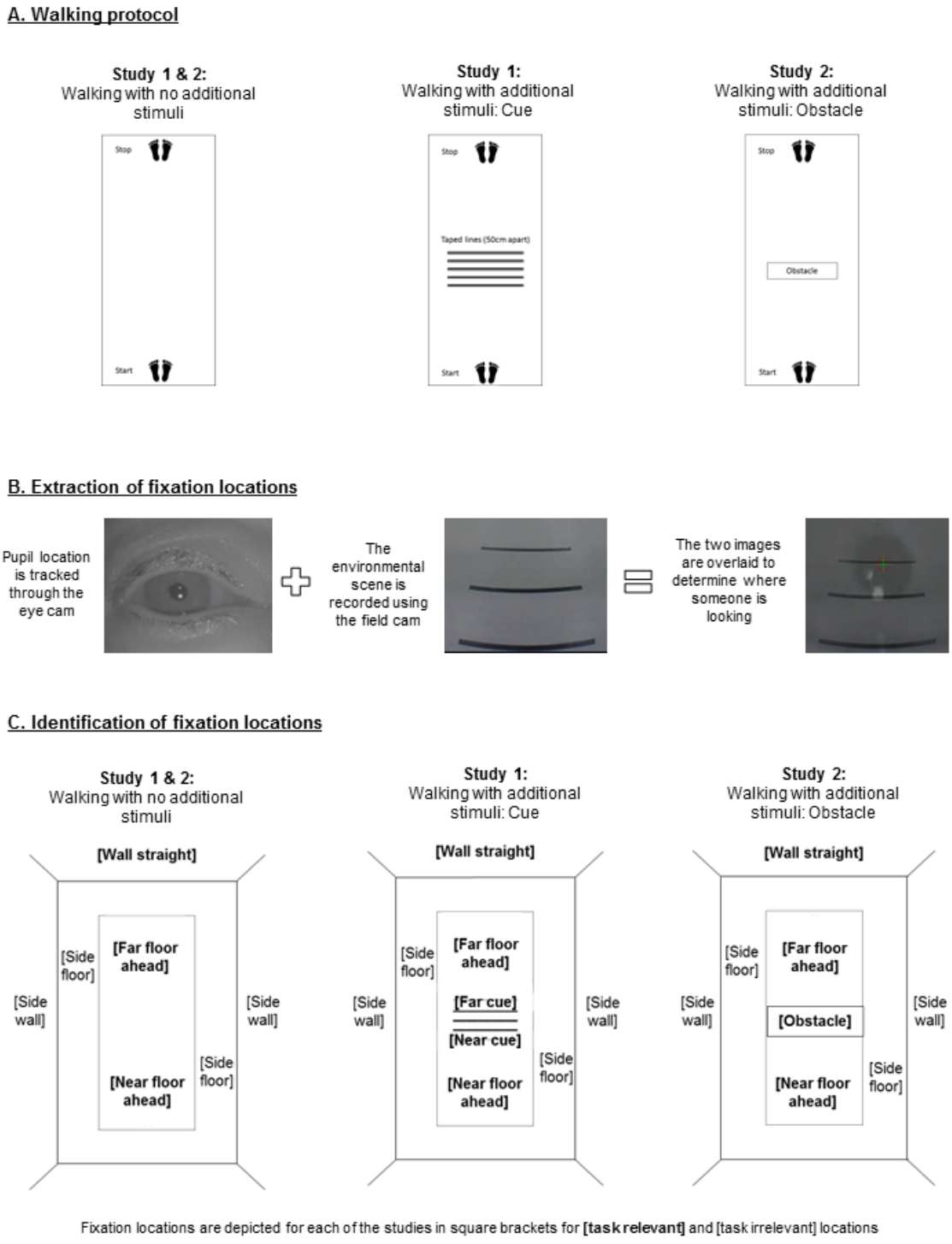

Figure 1: Walking protocol (A), extraction (B) and identification (C) of fixation location

2.5 Equipment and calibration

Eye movements were tracked using a Dikablis infrared mobile eye-tracker (Ergoneers GmbH, Germany) which uses synchronised video footage from two head-mounted cameras sampling at 50Hz. A forward-facing camera captured the participant's visual scene and a monocular infrared camera recorded the movements of the left

eye (Figure 1B). The manufacturer's software (Dikablis Recorder v2.5) detected the pupil position using inbuilt algorithms relying upon the relative blackness of the pupil. This data was exported as XY co-ordinates. System calibration was completed per participant prior to data acquisition to ensure that the camera views had been overlaid correctly.

2.6 Data analysis

Eye-tracking data from the first trial of each condition were analysed as visual exploration was considered most natural when participants were naïve to the environmental condition. Raw co-ordinate data were cropped to the trial duration (start and end of walking). Frame-by-frame manual interpolation and error correction were completed in the Dikablis Analysis software to correct instances in which the eye-tracker failed to locate the pupil correctly. The cleaned video files were down-sampled to 25Hz automatically by the Dikablis software and were input through a custom algorithm to extract visual fixations using MATLAB® (R2015a, The MathWorks Inc., Natick, MA, USA) [26]. The algorithm identified the first frame of a fixation which was exported as a static image (.jpeg). The image depicted the participants' visual scene with the cross-hair identifying the pupil location for each fixation.

Fixation locations were defined using our recently published classification scale [26], which are displayed in Table 1 and Figure 1C. The relevance of a fixation location was defined by its potential to provide useful visual information to enable safe completion of the complex walking task. Fixations were classified as task relevant if they were made on areas (i.e. floor, walls and stimuli) ahead of the participant in the trajectory of gait, or as task irrelevant if they were made to areas (i.e. floor, walls etc.) not in the participants' forward trajectory.

Table 1: Classification of fixations upon areas of interest[22]

Fixation Location	Definition
Task Relevant	
Wall Straight	The wall in front of the participant
Near Floor Ahead	The floor up to 2 meters ahead of the participant
Far Floor Ahead	The floor over 2 meters ahead of the participant
Near Cue (Study 1)	The cued area within 2 meters from the participant
Far Cue (Study 1)	The cued area beyond 2 meters from the participant
Obstacle (Study 2)	The obstacle
Task Irrelevant	
Side Wall	The walls to either side of the participant
Side Floor	The floor to either side of the participant
Ceiling	The ceiling

The same fixation locations were defined for both studies unless otherwise stated

2.7 Statistical analysis

Data were analysed in SPSS (v22, IBM Corp., Armonk, NY, USA) and normality was assessed for each group using one-sample Kolmogorov-Smirnov tests. Group means were compared using independent t-tests, analysis of variance or Mann-Whitney U tests accordingly, and categorical data was examined using Chi-squared tests. Tukey's test was used to identify outliers for fixation counts, and analysis with and without outliers was conducted to determine their influence. Since their inclusion did not yield differing results, outliers remain included within the analysis. Negative binomial regression was chosen to account for the over-dispersed count data (i.e. the data had more variability than a normal distribution), and was used for comparison of fixation counts. The Wald chi squared ($\chi 2$) was reported. It was also used in a backwards step wise model to examine for factors influencing fixation location when walking (age, sex, time in education, visual acuity and contrast sensitivity (binocular, monocular and absolute difference), MMSE total score, PD disease duration, Hoehn & Yahr disease stage, UPDRS III score and self-reported fear of falling), with the model's goodness of fit accepted with a Residual Deviance of 0.9-1.1. Factors were removed from the model until the strongest model remained. The number of task irrelevant fixations were sufficiently low (<2 excluding outliers for both groups under all conditions) that they did not fit the model, and were transformed into a binary data set (no irrelevant fixations made, one or more irrelevant fixations made) and subsequently analysed categorically using the

Pearson chi squared statistic. The Incident-Rate Ratio (IRR) was used to indicate whether more (IRR>1) or fewer (IRR<1) fixations were made for any significant associations. Significance was accepted at $p<0.05$.

3. Results

3.1 Participant demographic analysis

Data from two PD and one control participant were excluded due to equipment failure, whilst an additional two PD participants' data were removed as they were unable to complete the study protocol due to freezing of gait. Final analyses included 38 PD and 40 control participants for the straight walking trials. Initial analysis of both demographic and fixation location data revealed no significant differences between Study 1 and Study 2 cohorts for either PD or control groups, so they were collapsed into a single PD and control group for analysis of walking (Table 2, PD n=38, Control n=40). The PD and control groups did not significantly differ with respect to age ($p=0.532$) or sex ($p=0.350$) and thus were not controlled for in the statistical analyses. Those with PD had spent significantly less time in education and had poorer global cognition (MMSE, $p<0.001$). Spearman rho correlations were used to further assess whether global cognition or education were significantly associated with fixation location (task relevant or task irrelevant). Of the 48 correlations assessed, only one reached statistical significance highlighting a correlation between global cognition and task relevant fixations during obstacle crossing in the PD group ($rho=.495$, $p<.05$). Thus it was concluded that neither variable had a significant influence upon fixation location and were not controlled for within our subsequent analysis.

Table 2: Participant Demographics

Characteristic	PD (n=38)	Control (n=40)	Statistic	*P*
Age (years)[1]	69.6 (8.2)	68.4 (8.8)	t_{76} = -0.627	0.532
Sex (male/female)	23m / 15f	20m / 20f	χ^2_1 = 0.873	0.350
Time in Education (years)[2]	12.0 (10.0-14.5)	14.0 (12.0-17.0)	U = 432.0	**0.001***
MMSE (Score/30)[2]	28.5 (27.0-29.0)	30.0 (29.0-30.0)	U = 361.0	<**0.001***
Bilateral Visual Acuity (LogMAR)[1]	0.0 (0.2)	0.1 (0.1)	t_{76} = -2.982	**0.004***
Bilateral Contrast Sensitivity (LogCS)[1]	1.5 (0.2)	1.6 (0.1)	t_{50} = 3.778	<**0.001***
PD Disease Duration (years)[1]	7.3 (6.7)	-		-
Hoehn & Yahr Disease Stage	I (6)			
	II (25)	-		-
	III (7)			
UPDRS III (Score/56)[1]	32.0 (16.2)	-		-
Fear of falling (FES-I; Score/64) [1]	31.2 (10.6)			

'*' denotes significance ($p<0.05$), [1] Denotes Mean (SD), [2] denotes Median (IQR). Independent *t*-tests, chi-squared tests and Mann-Whitney *U* tests were used for between group comparisons of demographic data.

3.2 Fixation Location Analysis

3.2.1 Location of fixations in PD and controls when walking

The locations of fixations made in all walking trials are shown in Table 3. In the level walking trials there were no significant differences in the total or task relevant fixations between groups, however participants with PD made significantly more task irrelevant fixations ($p=0.014$).

Table 3: Relevance of fixation locations during each of the walking conditions

Walking without additional stimuli				
Fixation Count	**PD (n=38)**	**Control (n=40)**	**χ^2**	***P***
Total	3.45 (3.40)	2.40 (1.37)	4.604[1]	**0.032***
Task Relevant	2.55 (2.00)	2.30 (1.22)	0.483[1]	0.487
Task Irrelevant	0.89 (2.50)	0.10 (0.38)	6.087[2]	**0.014***
Walking with additional stimuli – Study 1: Visual Cueing				
Fixation Count	**PD (n=20)**	**Control (n=21)**	**χ^2**	***P***
Total	4.75 (2.92)	4.38 (2.42)	0.213[1]	0.645
Task Relevant	4.70 (2.94)	4.14 (2.26)	0.511[1]	0.475
Task Irrelevant	0.05 (0.22)	0.24 (0.54)	1.764[2]	0.359
Walking with additional stimuli – Study 2: Obstacle crossing				
Fixation Count	**PD (n=18)**	**Control (n=19)**	**χ^2**	***P***
Total	4.22 (2.34)	2.42 (0.90)	8.864[1]	**0.003***
Task Relevant	3.83 (2.33)	2.26 (0.93)	7.357[1]	**0.007***
Task Irrelevant	0.39 (1.04)	0.16 (0.37)	0.004[2]	1.000

'*' denotes significance ($p<0.05$), [1] Denotes analysis using Wald χ^2 (df = 1), [2] denotes analysis using Pearson χ^2 (df = 1). Data are presented as 'Mean (SD)'.

3.2.2 Location of fixations in PD and controls when walking with visual cues and salient obstacles

The effect of visual cues and the obstacle on fixation locations are displayed through difference scores (fixations made when walking with additional stimuli (i.e., obstacle or cue) – fixations made when walking) in Figure 2. When walking with visual cues, more task relevant fixations were made by both groups compared to walking. The increased task irrelevant fixations seen in PD during walking were corrected with visual cues present. With an obstacle present, PD made significantly more task relevant fixations than controls. Again, the previous difference observed in task irrelevant fixations between groups was not observed with the obstacle present.

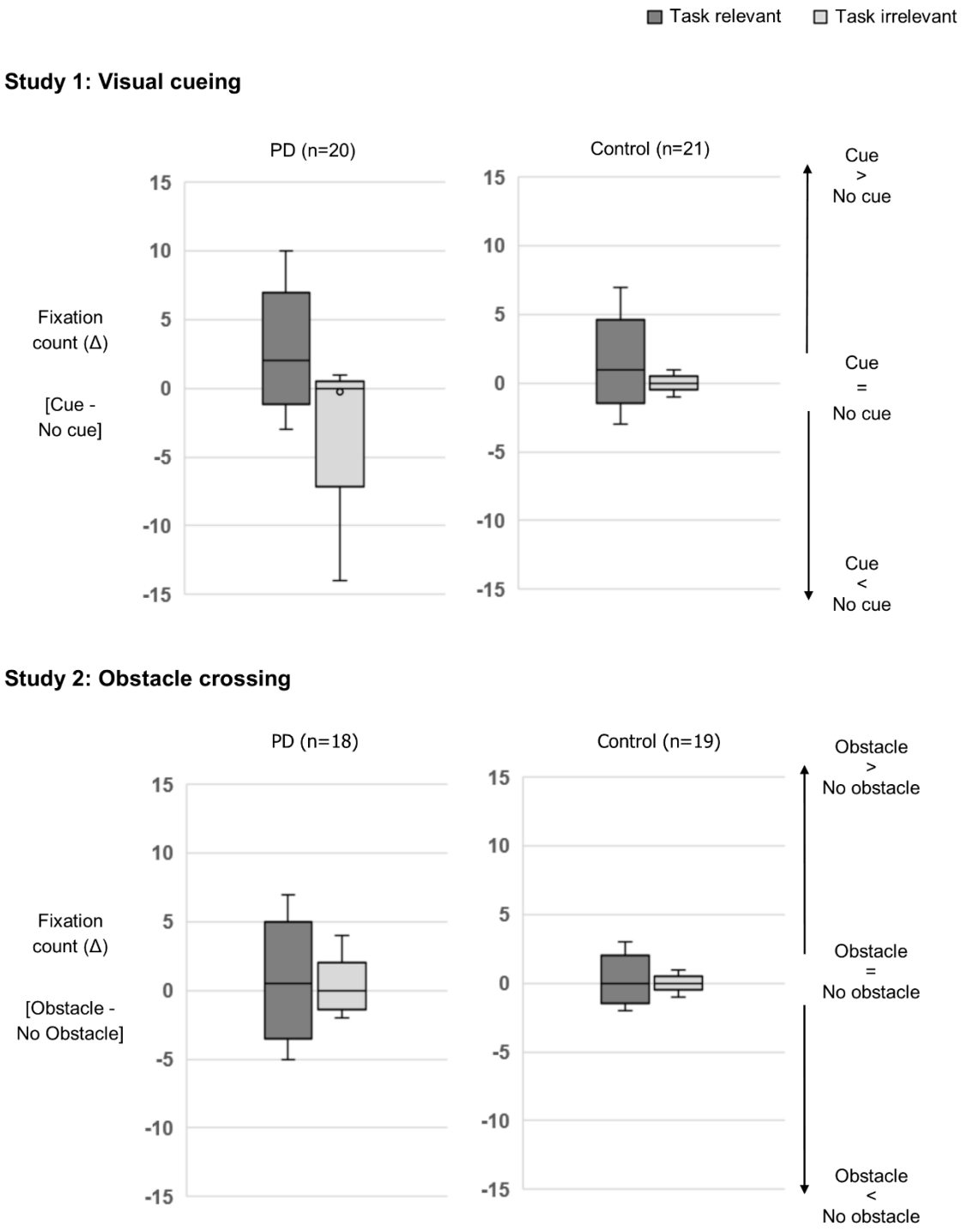

Figure 2: The effect of additional stimuli on the relevance of visual fixations. Difference scores (Walking with additional stimuli – walking without additional stimuli) were calculated and displayed for task relevant and task irrelevant fixations in PD and control participants.

3.3 Factors underpinning fixation location and relevance

Table 4 shows the factors significantly influencing the total, task relevant and irrelevant fixations made in walking trials (Study 1 and Study 2 groups collapsed). All demographic, visual, cognitive and PD-specific outcomes were entered into the negative binomial regression model which assessed the contribution of each outcome to the model and included only the outcomes which substantially contributed to the strongest model. No significant associations (i.e. no combinations of factors resulted in $p<0.05$) for the control group. In the PD group, a reduction in bilateral visual acuity (increase in LogMAR score) predicted: fewer total fixations ($\chi2=6.238$, $p=0.013$) and fewer task relevant fixations ($\chi2=3.384$, $p=0.066$). Visual acuity scores increased as fixation count decreased, with the IRR indicating reducing fixation counts for those with higher scores and therefore poorer visual acuity and contrast sensitivity. Years of education, sex, global cognition (MMSE) or a fear of falling (FES-I) did not make a significant contribution to the regression model.

Table 4: Significant factors influencing fixations made in walking trials with no additional stimuli.

	Fixation Count	Factor(s)	Wald χ^2 (df = 1)	Deviance	*P*	IRR
Control (n=40)	Total	Age	2.924	0.643	0.087	
		VA Abs Diff	3.213		0.073	
	Task Relevant	Age	2.162	0.566	0.141	
		VA Abs Diff	2.280		0.131	
	Task Irrelevant	Age	1.353	0.326	0.245	
		VA Abs Diff	1.808		0.179	
PD (n=38)	Total	Bilateral VA	6.238	0.954	**0.013***	0.102
	Task Relevant	Bilateral VA	3.384	1.082	0.066	
	Task Irrelevant	Disease Duration	2.727	0.699	0.099	

'*' Denotes significance ($p<0.05$). VA = Visual Acuity, Abs Diff = Absolute difference, Incident-Rate Ratio = IRR.

4. Discussion

This study explored the location and task relevance of visual fixations during walking in different contexts. Novel findings include inefficient visual exploration in people with PD compared to controls which improved in the presence of visual cues or a salient obstacle. PD participants who had reduced visual acuity were also likely to make fewer fixations whilst walking.

4.1 Mechanisms underpinning inefficient visual exploration in PD

Inefficient visual exploration in PD when walking may be caused by differences in acquisition of visual information leading to difficulties in correctly identifying and recognising task relevant stimuli. Both visual acuity and contrast sensitivity were impaired in PD as expected from previous literature [3,27]. Reduced inhibition of reflexive eye movements may also have contributed to the inefficiencies observed. Saccades towards an area of interest can be characterised as voluntary or reflexive, depending on whether the movement was executed deliberately. A failure to inhibit reflexive eye movements which is well documented in PD [6,13], may contribute to the increased number of irrelevant fixations. This is supported by the recent characterisation of these eye movements in PD due to disease-related pathology in the retino-colliculo-thalamo-amygdala pathway [28]. Reduced control of reflexive saccades is associated with disease progression [29] such that impairments in visual exploration are likely to be exacerbated in more advanced PD compared to the relatively mild group included in the present study. Acquisition of visual information is to some extent under cognitive control, therefore impaired cognition could explain inappropriate fixations. The relationship between vision and cognition in PD has been described [30,31], especially the mediating role of attention [32]. Attentional impairment is common in PD and may therefore increase the proportion of irrelevant fixations. Although we didn't find an association with cognition, this is probably due to the limitations of the cognitive test (MMSE) and the relatively mild PD group included in the present study. Environmental modifications, such as improved contrast of ground-based hazards and visual cues, may be useful to guide vision (and thus attention) even in the presence of the deficits seen in PD.

4.2 The effect of environmental stimuli

Visual cues and salient obstacles guided vision towards task relevant areas thus correcting the inefficiencies in visual exploration that we observed in people with PD when walking without additional stimuli. This enhances our understanding of the mechanisms underpinning their utility. Whilst visual cues have been shown to be beneficial for ameliorating gait deficits in people with PD [33-35], their effect on guiding vision during cued walking may be of importance. Given that people with PD who have more severe symptoms make a greater number of fixations when walking with visual cues [11], they may have greater benefits as the disease progresses. In addition, the increase in overall fixation count in obstacle crossing trials suggests that the ability

to perceive salient stimuli may be impaired in PD and more fixations may be required for sufficient understanding of the environment. People with PD often present with impaired visuospatial ability and working memory [36] which will likely have influenced the ability to perceive the salient obstacle, meaning more fixations were required to acquire and retain sufficient information to traverse it. This has also been demonstrated in previous research highlighting that PD are more reliant on visual information during obstacle crossing than age-matched controls [37]. It is plausible that people with good peripheral vision may have not needed to fixate upon the actual cue or obstacle to obtain sufficient visual information for task completion. People with PD experience neurodegeneration to retinal cells [2] and photoreceptors [38] and consequently the quality of their peripheral vision may also be adversely affected. Assessment of peripheral and central field vision loss during routine clinical assessments with PD would be beneficial.

4.3 Factors influencing visual exploration

To our knowledge this is the first study to examine the effect of clinical outcomes on the contextual relevance of visual exploration. Reduced bilateral visual acuity predicted fewer total and task relevant fixations when walking in PD which may lead to reduced visual exploration. Whilst visual acuity was associated with the context of fixations in PD, it must acknowledged that the majority of participants had good visual acuity with only four PD participants scoring less than that required for driving. Consequently, further work may consider the role of vision and context of visual information acquired during locomotor tasks in individuals with greater visual impairments. Contrast sensitivity was not significantly associated with fixation pattern, although it may not be challenged adequately in a laboratory environment. Furthermore, the model fit was not as good as for other variables, and would likely be improved in future research using a longer walk of greater complexity (i.e. cluttered environments).

Global cognition (i.e. MMSE total score) did not significantly influence visual exploration contrary to our hypothesis. Although the MMSE is a good screening tool for cognitive impairment, it may not be sensitive to milder cognitive impairment in PD with less severe disease [39], and future research would benefit from more rigorous cognitive assessment. Furthermore the narrow range of MMSE scores in the entire cohort (27-30)

likely influenced its utility for predicting fixation outcomes and future research should include a group of PD participants with a larger range of cognitive function.

4.4 Implications for Clinical Practice and Future Research

The present study found differences in visual exploration in PD compared to age-matched controls during walking and obstacle crossing. Implementing environmental modifications such as visual cues and improving the contrast of ground-based obstacles appears to positively alter visual exploration by reducing the number of irrelevant fixations. For practical implementation, visual cues need to be tested over time to understand how to optimise cue type to best suit the individual (i.e. location, type, duration, interval, colour-contrast), how to vary the cue type to prevent habituation and how visual exploration is modified in response to cue type. Whilst the contrast of potential trip hazards (i.e. obstacles) appears to guide vision towards these important areas, research exploring a range of obstacle sizes and contrasts may help to determine the optimal way to highlight these important environmental features to reduce falls risk. Both potential interventions should also be explored in real-world environments to better simulate and evaluate a home-based intervention.

These interventions may provide even further benefit than this exploratory work indicates due to the influence of antiparkinsonian medication on vision [40]. As the effect of dopaminergic medication wears off and people with PD experience motor fluctuations, visual function (i.e. acuity and contrast sensitivity) and exploration (i.e. saccades and fixations) may also become less effective. Consequently, the differences exposed in this study may be exacerbated when people with PD are not optimally medicated. As such, these interventions may have greater utility for improving visual exploration when dopaminergic medication is not optimal. Assessing the effect of medication on visual exploration during ambulatory tasks is also recommended for future work.

Furthermore, these subsequent studies will benefit from automated area of interest analysis and superior spatial resolution of the field camera, as this will allow for accurate and efficient classification of fixations in smaller areas of interest within more complex visual environments. Increased temporal resolution of the apparatus to

at least 200Hz will allow more accurate measurement of the velocity, direction and latency of saccades during locomotion[41,42], thereby providing a better understanding of visual exploration.

5. Conclusions

Reduced efficiency of visual exploration when walking is likely to influence the safety of people with PD during locomotor tasks and increase overall disease morbidity. Visual exploration was redirected to relevant areas when guided by visual cues or a high contrast obstacle, and as such may prove to be a useful home-based modification to improve locomotor safety and reduce falls risk in people with PD. Further research exploring how improving the saliency of task relevant stimuli may be optimised to the individual is required so that falls interventions may be implemented in the home environments.

References

1. Weil, R.S., A.E. Schrag, J.D. Warren, S.J. Crutch, A.J. Lees, and H.R. Morris, Visual dysfunction in Parkinson's disease. Brain, 2016.
2. Archibald, N.K., M.P. Clarke, U.P. Mosimann, and D.J. Burn, The retina in Parkinson's disease. Brain, 2009. 132(5): p. 1128-1145.
3. Davidsdottir, S., A. Cronin-Golomb, and A. Lee, Visual and spatial symptoms in Parkinson's disease. Vision Research, 2005. 45(10): p. 1285-1296.
4. Galna, B., S. Lord, D. Daud, N. Archibald, D. Burn, and L. Rochester, Visual sampling during walking in people with Parkinson's disease and the influence of environment and dual-task. Brain Research, 2012. 1473: p. 35-43.
5. Tatler, B.W., Current understanding of eye guidance. Visual Cognition, 2009. 17(6-7): p. 777-789.
6. Chan, F., I.T. Armstrong, G. Pari, R.J. Riopelle, and D.P. Munoz, Deficits in saccadic eye-movement control in Parkinson's disease. Neuropsychologia, 2005. 43(5): p. 784-796.
7. Stuart, S., B. Galna, L.S. Delicato, S. Lord, and L. Rochester, Direct and indirect effects of attention and visual function on gait impairment in Parkinson's disease: influence of task and turning. European Journal of Neuroscience, 2017. 46(1): p. 1703–1716.
8. Archibald, N.K., S.B. Hutton, M.P. Clarke, U.P. Mosimann, and D.J. Burn, Visual exploration in Parkinson's disease and Parkinson's disease dementia. Brain, 2013. 136(3): p. 739-750.
9. Vitório, R., L.T.B. Gobbi, E. Lirani-Silva, R. Moraes, and Q.J. Almeida, Synchrony of gaze and stepping patterns in people with Parkinson's disease. Behavioural Brain Research, 2016. 307: p. 159-164.
10. Vitório, R., E. Lirani-Silva, F. Pieruccini-Faria, R. Moraes, L.T.B. Gobbi, and Q.J. Almeida, Visual cues and gait improvement in Parkinson's disease: Which piece of information is really important? Neuroscience, 2014. 277: p. 273-280.
11. Beck, E.N., K.A. Ehgoetz Martens, and Q.J. Almeida, Freezing of Gait in Parkinson's Disease: An Overload Problem? PLoS ONE, 2015. 10(12): p. e0144986.
12. Goodale, M.A. and A.D. Milner, Separate visual pathways for perception and action. Trends in Neurosciences, 1992. 15(1): p. 20-25.
13. Amador, S.C., A.J. Hood, M.C. Schiess, R. Izor, and A.B. Sereno, Dissociating cognitive deficits involved in voluntary eye movement dysfunctions in Parkinson's disease patients. Neuropsychologia, 2006. 44(8): p. 1475-1482.
14. Nieuwboer, A., et al., Cueing training in the home improves gait-related mobility in Parkinson's disease: the RESCUE trial. Journal of Neurology, Neurosurgery & Psychiatry, 2007. 78(2): p. 134-140.
15. Gazibara, T., T. Pekmezovic, D.K. Tepavcevic, A. Tomic, I. Stankovic, V.S. Kostic, and M. Svetel, Circumstances of falls and fall-related injuries among patients with Parkinson's disease in an outpatient setting. Geriatric Nursing, 2014. 35(5): p. 364-369.
16. Stuart, S., B. Galna, S. Lord, and L. Rochester, A protocol to examine vision and gait in Parkinson's disease: impact of cognition and response to visual cues. F1000Research, 2015. 4.

17. Mirelman, A., et al., V-TIME: a treadmill training program augmented by virtual reality to decrease fall risk in older adults: study design of a randomized controlled trial. BMC Neurology, 2013. 13(1): p. 15.

18. Alcock, L., B. Galna, J.M. Hausdorff, S. Lord, and L. Rochester, Gait & Posture Special Issue: Gait adaptations in response to obstacle type in fallers with Parkinson's disease. Gait & posture, 2018.

19. World Medical Association, World medical association declaration of helsinki: Ethical principles for medical research involving human subjects. JAMA, 2013. 310(20): p. 2191-2194.

20. Hughes, A.J., S.E. Daniel, L. Kilford, and A.J. Lees, Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. Journal of Neurology, Neurosurgery & Psychiatry, 1992. 55(3): p. 181-184.

21. Hoehn, M.M. and M.D. Yahr, Parkinsonism: onset, progression and mortality. Neurology, 1967. 17(5): p. 427-42.

22. Folstein, M.F., S.E. Folstein, and P.R. McHugh, "Mini-mental state": A practical method for grading the cognitive state of patients for the clinician. Journal of Psychiatric Research, 1975. 12(3): p. 189-198.

23. Goetz, C.G., et al., Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale presentation and clinimetric testing results. Movement Disorders, 2008. 23(15): p. 2129-2170.

24. Howard, I.P. and B.J. Rogers, Binocular vision and stereopsis. 1995, USA: Oxford University Press.

25. Yardley, L., N. Beyer, K. Hauer, G. Kempen, C. Piot-Ziegler, and C. Todd, Development and initial validation of the Falls Efficacy Scale-International (FES-I). Age and ageing, 2005. 34(6): p. 614-619.

26. Stuart, S., D. Hunt, J. Nell, A. Godfrey, J.M. Hausdorff, L. Rochester, and L. Alcock, Do you see what I see? Mobile eye-tracker contextual analysis and inter-rater reliability. Medical & Biological Engineering & Computing, 2017: p. 1-8.

27. Archibald, N.K., M.P. Clarke, U.P. Mosimann, and D.J. Burn, Visual symptoms in Parkinson's disease and Parkinson's disease dementia. Movement Disorders, 2011. 26(13): p. 2387-2395.

28. Diederich, N.J., G. Stebbins, C. Schiltz, and C.G. Goetz, Are patients with Parkinson's disease blind to blindsight? Brain, 2014. 137(6): p. 1838-1849.

29. Anderson, T.J. and M.R. MacAskill, Eye movements in patients with neurodegenerative disorders. Nature Reviews Neurology, 2013. 9(2): p. 74-85.

30. Helmich, R.C., L.C. Derikx, M. Bakker, R. Scheeringa, B.R. Bloem, and I. Toni, Spatial Remapping of Cortico-striatal Connectivity in Parkinson's Disease. Cerebral Cortex, 2010. 20(5): p. 1175-1186.

31. Stuart, S., S. Lord, E. Hill, and L. Rochester, Gait in Parkinson's disease: A visuo-cognitive challenge. Neuroscience & Biobehavioral Reviews, 2016. 62: p. 76-88.

32. Petersen, S.E. and M.I. Posner, The Attention System of the Human Brain: 20 Years After. Annual Review of Neuroscience, 2012. 35: p. 73-89.

33. Rochester, L., V. Hetherington, D. Jones, A. Nieuwboer, A.-M. Willems, G. Kwakkel, and E. Van Wegen, The effect of external rhythmic cues (auditory and visual) on walking during a functional task in homes of people with Parkinson's disease. Archives of physical medicine and rehabilitation, 2005. 86(5): p. 999-1006.

34. Lewis, G.N., W.D. Byblow, and S.E. Walt, Stride length regulation in Parkinson's disease: the use of extrinsic, visual cues. Brain, 2000. 123(10): p. 2077-2090.

35. Azulay, J.-P., S. Mesure, and O. Blin, Influence of visual cues on gait in Parkinson's disease: contribution to attention or sensory dependence? Journal of the neurological sciences, 2006. 248(1): p. 192-195.

36. Pagonabarraga, J. and J. Kulisevsky, Cognitive impairment and dementia in Parkinson's disease. Neurobiology of Disease, 2012. 46(3): p. 590-596.

37. Vitório, R., E. Lirani-Silva, F.A. Barbieri, V. Raile, F. Stella, and L.T.B. Gobbi, Influence of visual feedback sampling on obstacle crossing behavior in people with Parkinson's disease. Gait & Posture, 2013. 38(2): p. 330-334.

38. Roth, N.M., et al., Photoreceptor layer thinning in idiopathic Parkinson's disease. Movement Disorders, 2014. 29(9): p. 1163-1170.

39. Zadikoff, C., et al., A comparison of the mini mental state exam to the montreal cognitive assessment in identifying cognitive deficits in Parkinson's disease. Movement Disorders, 2008. 23(2): p. 297-299.

40. Ekker, M.S., et al., Ocular and visual disorders in Parkinson's disease: Common but frequently overlooked. Parkinsonism & Related Disorders, 2017. 40: p. 1-10.

41. Holmqvist, K., M. Nyström, R. Andersson, R. Dewhurst, H. Jarodzka, and J. Van de Weijer, Eye tracking: A comprehensive guide to methods and measures. 2011, Oxford: Oxford University Press.

42. Stuart, S., L. Alcock, B. Galna, S. Lord, and L. Rochester, The measurement of visual sampling during real-world activity in Parkinson's disease and healthy controls: A structured literature review. J Neurosci Methods, 2013.